



Numenos AI, unleashing the power of clinical data

Pioneering the use of **clinico-genomic
foundation** models for drug discovery

CURE Dermatology outperforms DEG analysis in Atopic Dermatitis RWD Analysis

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Abstract

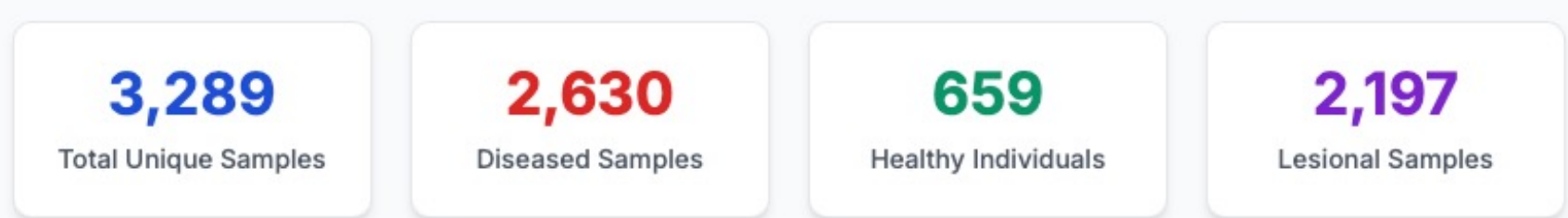
Numenos developed a new type of deep learning platform that predicts patient response to cancer therapies. The large clinico-genomic model (LCGM), created by Numenos, is called Clinical trials Uncovering Real Efficacy Artificial Intelligence (CURE AI). CURE AI is trained on a large collection of clinico-genomic datasets (>500,000 patients) to learn the complex relationships between the vast clinical and multiomic features in clinical trial data. Key innovations include: 1) A specialized deep learning architecture optimized for clinical trial data analysis; and 2) A novel training approach using large-scale clinical genomics datasets to enable accurate benefit prediction. However, we do not yet know of the potential limits of utilizing cross-cancer and pan-cancer predictions of immunotherapy response. In this study, for the first time, we assess how well CURE AI can be finetuned on non-randomized real-world data to find new therapeutic targets for a non-malignant condition.

Using atopic dermatitis as a validation, we finetuned the base CURE AI model using over 800 atopic dermatitis samples and over 600 healthy control samples. The model was optimized to identify individualized genetic contributors to the pathologic condition (atopic dermatitis) and to prioritize individual gene/pathway contributors to the disease process. We also performed traditional differential gene expression (DEG) analysis as a comparison, in which normal and pathologic samples are grouped as cohorts, using RNA expression as the main input.

We found that while traditional DEG analysis identified a current atopic dermatitis-related gene target IL-13, it was found at #265 in the analysis. CURE AI, finetuned on atopic dermatitis, however identified IL-13 as a #9 overall hit. This is due to CURE AI being able to tease out the contributions of IL-13 to the disease process on an individualized basis, so for the patients to whom IL-13 is contributing (which CURE AI identifies), IL-13 is appropriately identified as a major pathologic contributor.

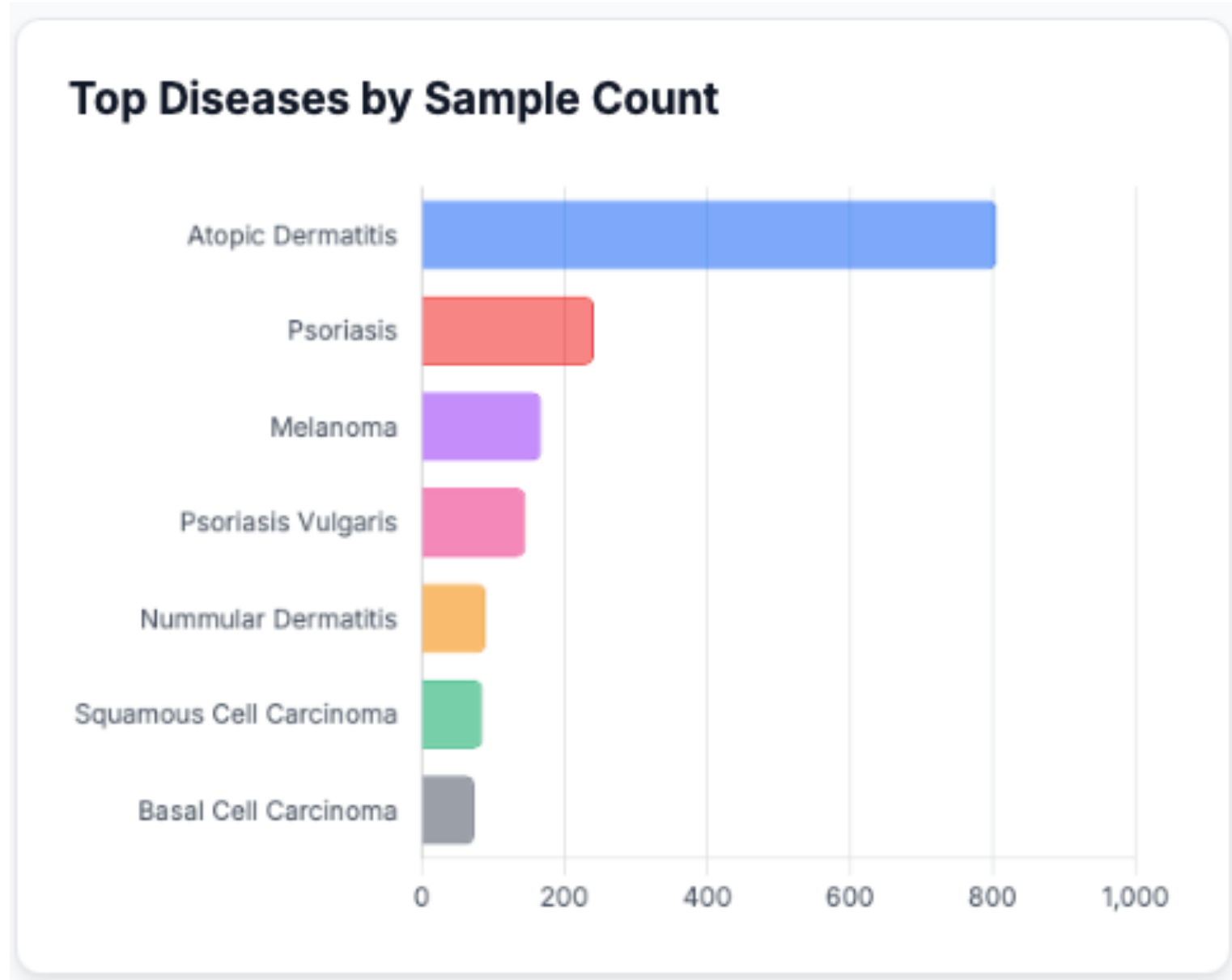
In summary, CURE AI can be finetuned on real-world data to identify drug targets of relevance to human disease.

Collected normal and pathological skin samples



Using similar real-world patient numbers, we can provide similar insights to any human disease, not just atopic dermatitis (which is highlighted below)..

Skin Disease Classification



IL-13 is a drug target in atopic dermatitis



DRUG NAME	TARGET / MECHANISM OF ACTION (MOA)	APPROVED FOR ATOPIC DERMATITIS
Dupilumab (Dupixent)	IL-4Ra (Blocks IL-4 & IL-13 signaling)	Yes
Lebrikizumab (Ebglyss)	Interleukin-13 (IL-13)	Yes
Nemolizumab (Nemluvio)	IL-31 Receptor α (IL-31Ra)	Yes
Traikininumab (Adbry)	Interleukin-13 (IL-13)	Yes
Vixarelimab	Oncostatin M Receptor β (OSMR β)	No
Amilteimab	OX40-Ligand (OX40L)	No
Fezakinumab	Interleukin-22 (IL-22)	No
Benralizumab (Fasenra)	IL-5 Receptor α (IL-5Ra)	No
Pitakinra	IL-4 Receptor α (IL-4Ra)	Development Discontinued

CURE AI, finetuned on atopic dermatitis samples from real-world data, identified a top current AD target as a top-10 hit.

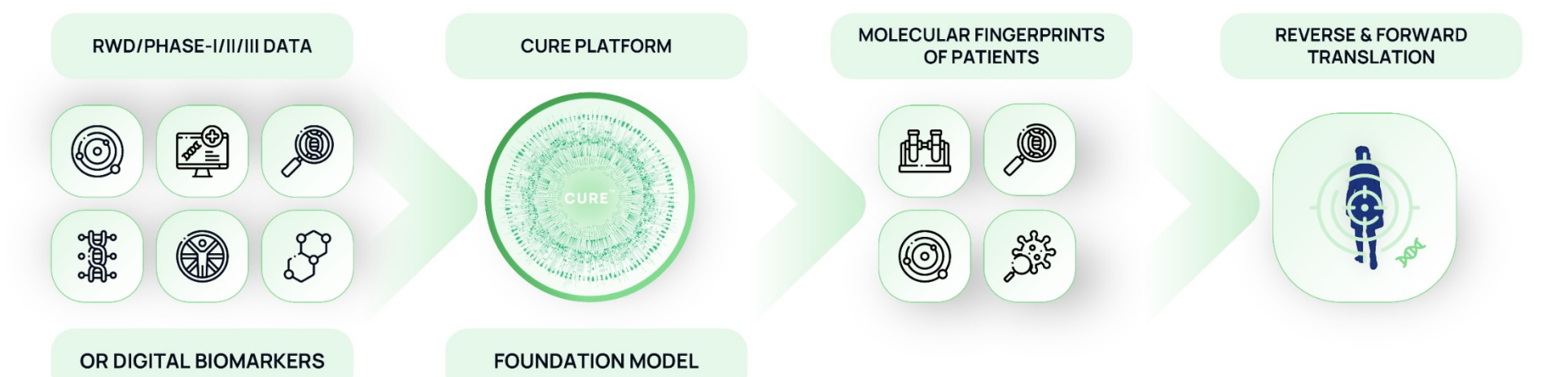
This suggests that CURE AI can be used to identify novel targets across a variety of other human pathologic conditions using real-world data.

CURE AI Biomarker Insights

CURE AI - trained on dermatology data - provides novel insights into dermatologic diseases.

CURE AI further can be optimized to deep-dive into the IL-13 benefiting populations for R&D insights including biomarker-defined patient selection.

One Solution, for any data type, or any indication



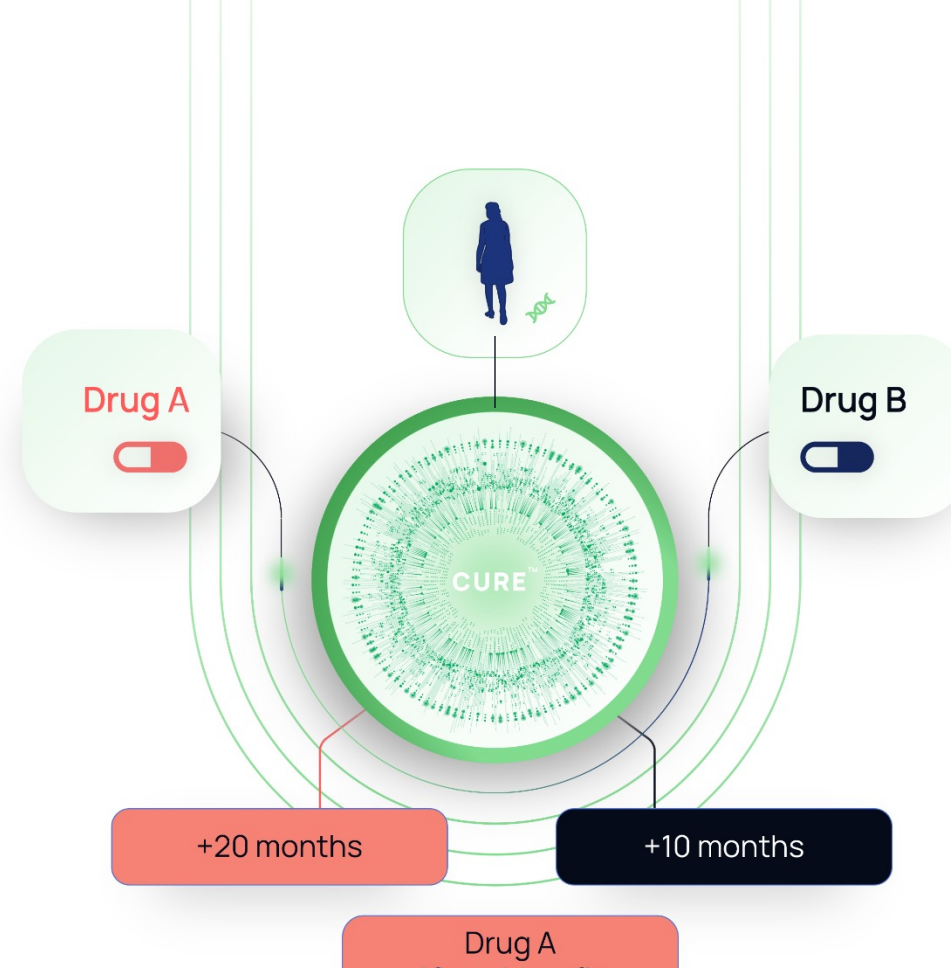
Input data can be a combination of client, public, or Numenos-acquired data

CURE AI predicts untaken drug effect for each patient

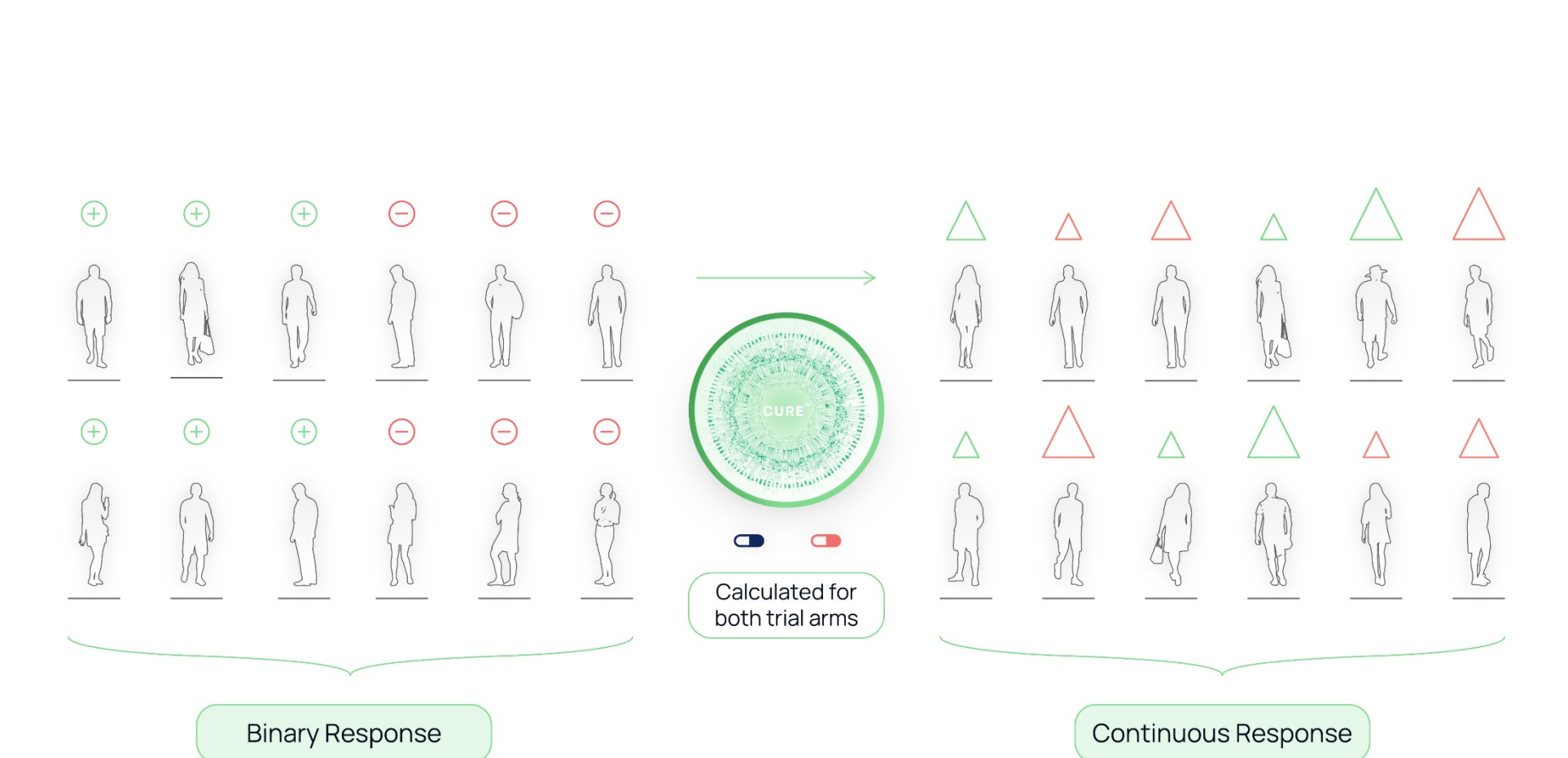
CURE AI calculates a counterfactual outcome for each patient to predict how they would have responded to the trial therapy that they did not receive.

The difference in this predicted outcome allows the creation of a continuous response measurement, allowing an ordering of patients by predicted clinical benefit.

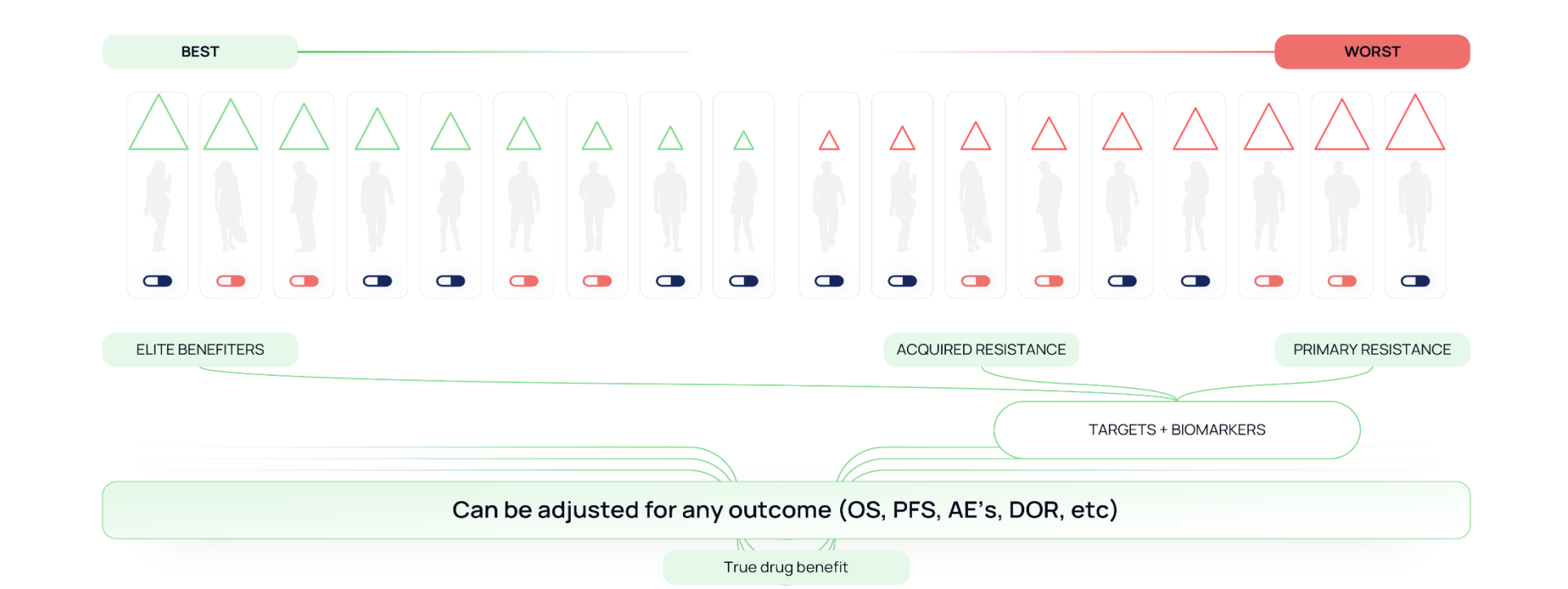
This allows us unparalleled insight into biomarker and target discovery, as we are able to minimize confounding variables.



CURE AI implements a Continuous Response Measurement

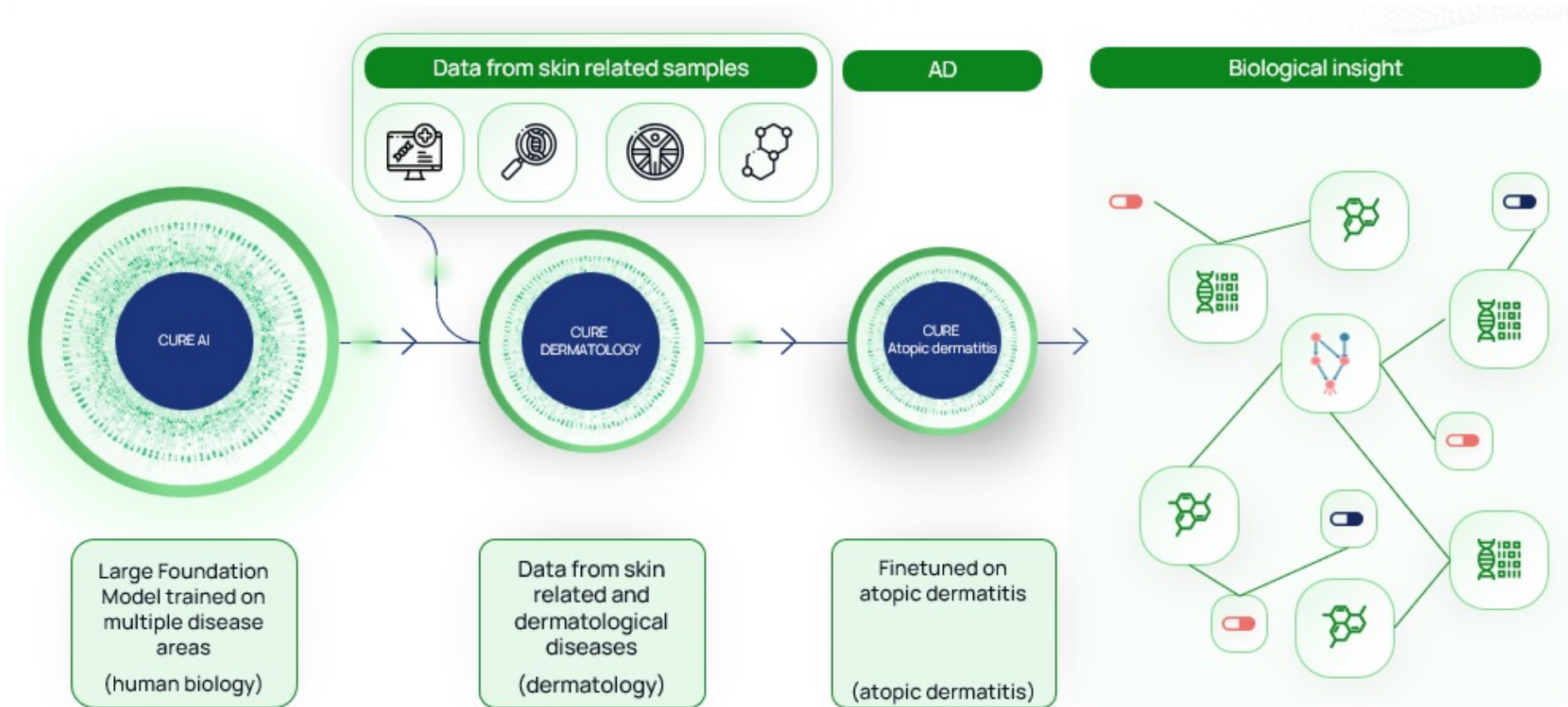


Comparing drug effects, not arms or responses!

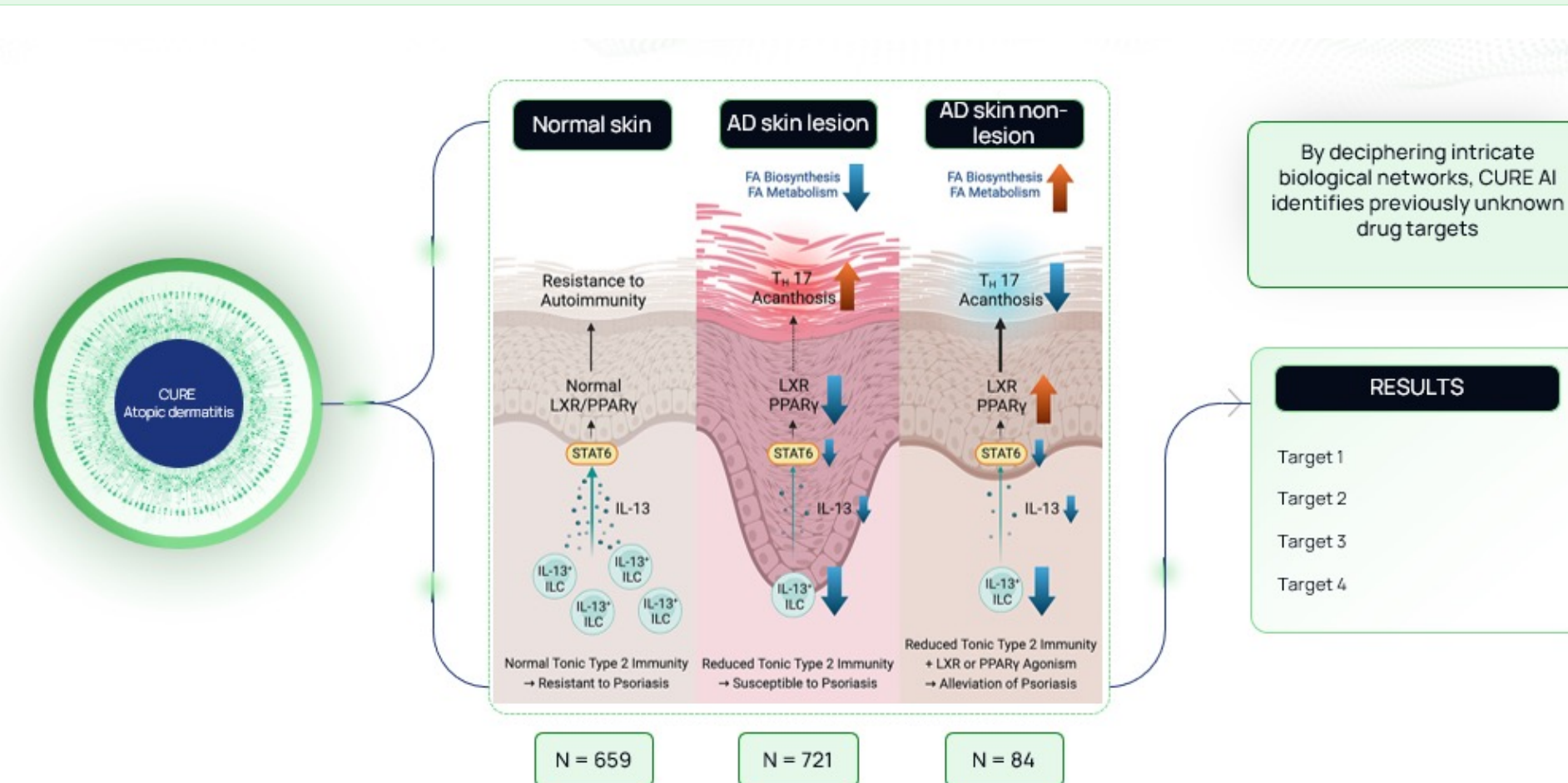


The ordering of patients by their CURE AI Score is called the CURE Index.

CURE Dermatology & CURE Atopic Dermatitis



Comparing normal and AD patients



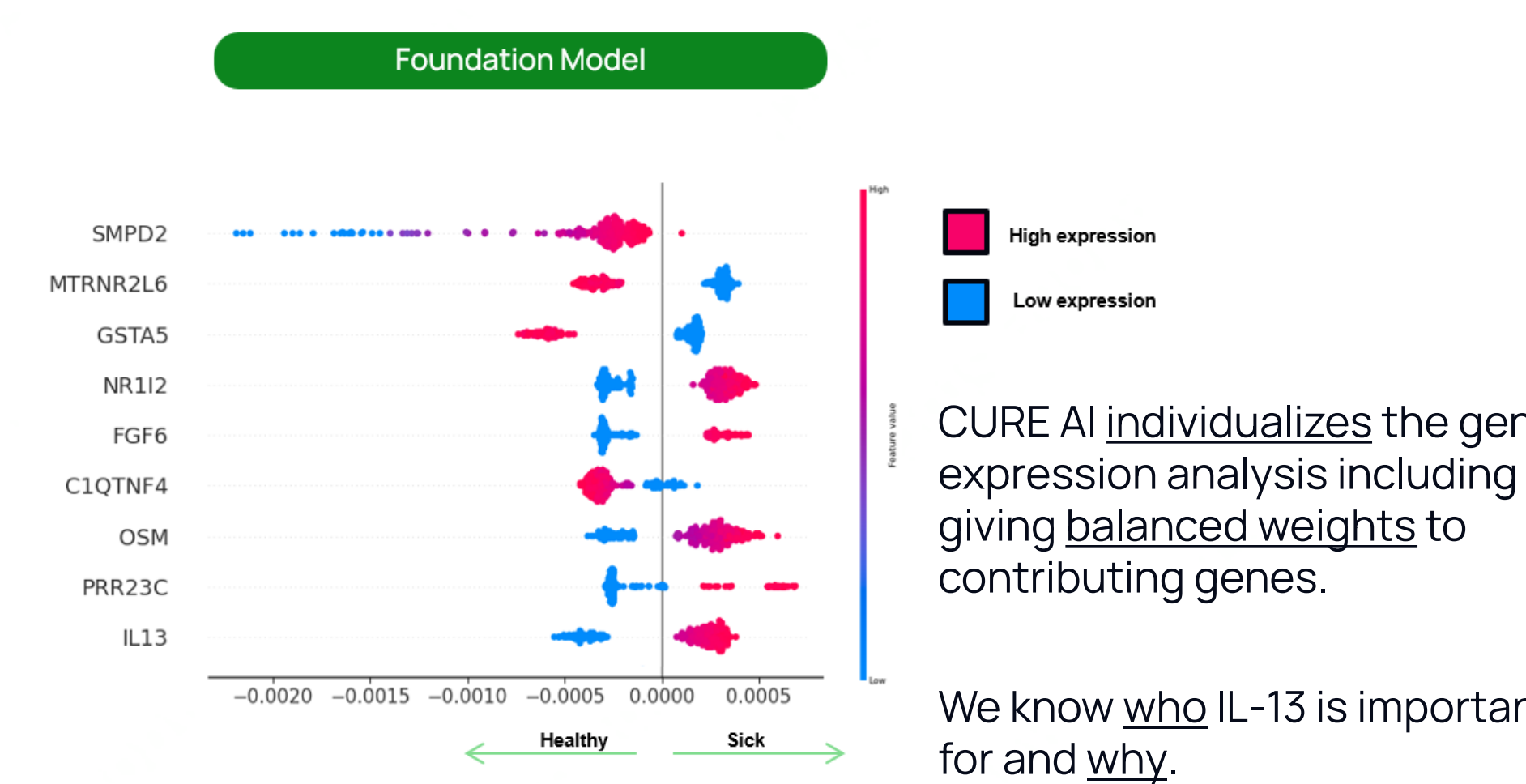
The OLD way: IL-13 is #265 hit for atopic dermatitis (AD)

Differential Gene Expression		
GENE SYMBOL	BASE MEAN	LOG2 FOLD CHANGE
LC3B3	12,114.98	+5.21
MTNR2L2	36,226.72	-8.49
MTNR2L6	922.01	-18.47
MTNR2L8	47,958.95	-7.78
N3R1244-3	3,489.41	-6.39
RAB6C	3,999.62	-6.57
LOC18377953	458.88	-8.99
AT9B8P	1,329.76	-6.73
LOC18798158	526.89	-7.53
N3R1244-4	2,627.52	-6.89

DEG analysis does not individualize analysis like CURE AI

Because results are averaged over cohorts, potentially significant results like IL-13 can be scattered among less likely contributing genes.

The CURE AI way: IL-13 is a top-10 hit



We know who IL-13 is important for and why.

CURE AI Indication Expansion

CURE AI can be utilized to understand which other dermatologic or autoimmune conditions could benefit from IL-13.

We can use your RWD to guide clinical trial eligibility for other diseases where an IL-13 or other existing target can be implemented for indication expansion.

Clinical Trial Potential

CURE AI is immediately available to guide clinical trial enrolment decisions

We also facilitate interim trial analysis and adaptive trial design.

Complete trial analysis can be completed in 6 weeks, facilitating rapid decision making for interim-trial design.

We provide real world, patient-level evidence for new therapy combinations and adaptive trial decisions.

CURE AI can be employed as a complex model as well as a simplified, distilled model for patient enrolment/recruitment.

Summary & Key Value Proposition

- Forward translation value**
 - Do not need your data to provide significant insights
 - Can identify biomarkers for patient enrichment resulting faster cheaper smaller trials
 - Indication expansion
 - Failure prevention
 - Interim analysis
- Reverse translation value**
 - Identify unmet need targets
 - Targets already come with identifiable patient population for enrichment for faster more efficient development

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